

CLAIMS

- 1. (Original) A method of treating a solid tumour in a subject, the method comprising the following steps
 - (i) delivering to the solid tumour a composition comprising an engineered ovine atadenovirus and a lipid; and
 - (ii) administering a prodrug to the subject,

wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts the prodrug to a cytotoxic metabolite, the gene being under the control of the promoter.

- 2. (Original) A method as claimed in claim 1 in which the promoter is selectively active in a specific tissue.
- 3. (Amended) A method as claimed in claim 1 or claim 2 in which the solid tumour is prostate cancer.
- 4. (Amended) A method as claimed in claim 2 or claim 3 1 in which the specific tissue is prostate tissue.
- 5. (Amended) A method as claimed in any one of claims 1 to 4 in which the promoter is a prostate specific membrane antigen promoter.
- 6. (Amended) A method as claimed in any one of claims 1 to 5 in which the promoter is a probasin promoter.

- 7. (Amended) A method as claimed in any one of claims 1-to 6 in which the ovine atadenovirus further comprises a transcriptional enhancer element.
- 8. (Original) A method as claimed in claim 7 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.
- 9. (Amended) A method as claimed in any one of claims 1 to 8 in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase/5-flurocytosine, human cytochrome P450/cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-flurouridine, cytosine kinase/cytosine arabinoside, *E. coli/GPT/* 6-thioxanthine,
- E. coli nitroreductase/5(-aziridine-l-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/6-methylpurine-2-deoxyriboside or fludarabine.
- 10. (Amended) A method as claimed in any one of claims 1 to 8 in which the enzyme is a purine nudeoside phosphorylase (PNP) and the prodrug is a purine prodrug which is converted by PNP to a toxic purine metabolite.
- 11. (Original) A method as claimed in claim 10 in which the prodrug is 6-methyl purine-2-deoxyriboside (6MPDR) or fludarabine.
- 12. (Amended) A method as claimed in any one of claims 1 to 11 in which the lipid is a cationic lipid.

13. (Amended) A method as claimed in any one of claims 1 to 12 in which the lipid is CSO87 having the formula:

14. (Amended) A method as claimed in any one of claims 1 to 12 which the lipid is CSO60 having the formula:

15. (Amended) A method as claimed in any one of claims 1 to 6 in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.

- 16. (Original) A composition comprising
 - (i) an engineered ovine atadenovirus; and
 - (ii) a lipid,

wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts a prodrug to a cytotoxic metabolite, the gene being under the control of the promoter.

- 17. (Original) A composition as claimed in claim 16 in which the promoter is selectively active in a specific tissue.
- 18. (Amended) A composition as claimed in claim 16 or claim 17 in which the promoter is a prostate specific membrane antigen promoter.
- 19. (Amended) A composition as claimed in any one of claims 16 to 18 in which the promoter is a probasin promoter.
- 20. (Amended) A composition as claimed in any one of claims 16 to 19 in which the ovine atadenovirus further comprises a transcriptional enhancer element.
- 21. (Original) A composition as claimed in claim 20 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.
- 22. (Amended) A composition as claimed in any one of claims 16 to 21 in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase/5-flurocytosine, human cytochrome P450/ cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-flurouridine, cytosine kinase/cytosine arabinoside, *E. coli* GPT/ 6-

thioxanthine, *E. coli* nitroreductase/5(-aziridine-1-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/6-methylpurine-2-deoxyriboside or fludarabine.

- 23. (Amended) A composition as claimed in any one of claims 16 to 21-in which the enzyme is a purine nucleoside phosphorylase (PNP) and the prodrug is a purine prodrug which is converted by PNP to a toxic purine metabolite.
- 24. (Original) A composition as claimed in claim 23 in which the prodrug is 6-methyl purine-2-deoxyriboside (6MPDR) or fludarabine.
- 25. (Amended) A composition as claimed in any one of claims 16 to 24 in which the lipid is a cationic lipid.
- 26. (Amended) A composition as claimed in any one of claims 16 to 25 in which the lipid is CSO87 having the formula:

27. (Amended) A composition as claimed in any one of claims 16 to 25 in which the lipid is CSO60 having the formula:

28. (Amended) A composition as claimed in any one of claims 16 to 27 in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.